Substitute Form PTO-1449 (Modified)	U.S. Department of Commerce Patent and Trademark Office	Attorney's Docket No.	Application No.
Information Disclosure Statement by Applicant (Use several sheets if necessary) (37 CFR §1.98(b))		01997-289001	09/933,638
		Applicant: Aleksey G. Kazantsev et al.	
		Filing Date: August 20, 2001	Group Art Unit

U.S. Patent Documents

Examiner Initial	Desig. ID	Patent Number	Issue Date	Patentee	Class	Subclass	Filing Date If Appropriate
	AA						
	AB						
	AC						
	AD						
	AE						
	AF						
	AG						
	AH						
	AI						
	AJ						
	AK						

Foreign Patent Documents or Published Foreign Patent Applications

Examiner Initial	Desig. ID	Document Number	Publication Date	Country or Patent Office	Class	Subclass	Translation Yes	Translation No
AO	AL	WO 93/15213 A1	05/08/93	WIPO				
AO	AM	WO 96/17956 A2	13/06/96	WIPO				
	AN							
	AO							
	AP							

Other Documents (include Author, Title, Date, and Place of Publication)

Examiner Initial	Desig. ID	Document
AO	AQ	Database GenCore, PCT-US01-26097-11.rsp
	AR	
	AS	
	AT	

Examiner Signature	Date Considered
	1/21/04

EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Substitute Form PTO-1449 (Modified)	U.S. Department of Commerce Patent and Trademark Office	Attorney's Docket No. 01997-289001	Application No. 09/933,638
Information Disclosure Statement by Applicant (Use several sheets if necessary) (37 CFR 1.98(b))		Applicant Aleksey G. Kazantsev et al.	
		Filing Date August 20, 2001	Group Art Unit

U.S. Patent Documents

Examiner Initial	Desig. ID	Patent Number	Issue Date	Patentee	Class	Subclass	Filing Date If Appropriate
	AA	6,015,555	01/18/2000	Friden			
	AB	5,994,392	11/30/1999	Shashoua			
	AC	5,328,470	07/12/1994	Nabel *et al.*			
	AD	5,144,011	09/01/1992	Shen *et al.*			

Foreign Patent Documents or Published Foreign Patent Applications

Examiner Initial	Desig. ID	Document Number	Publication Date	Country or Patent Office	Class	Subclass	Translation Yes	Translation No
	AE							

Other Documents (include Author, Title, Date, and Place of Publication)

Examiner Initial	Desig. ID	Document
	AF	Ambrose *et al.*, "Structure and Expression of the Huntington's Disease Gene: Evidence against Simple Inactivation Due to an Expanded CAG Repeat", *Somatic Cell and Molecular Genetics*, 20(1):27-38, 1994
	AG	Bates *et al.*, "Transgenic Mice in the Study of Polyglutamine Repeat Expansion Diseases", *Brain Pathology*, 8:699-714, 1998
	AH	Burright *et al.*, "SCA1 Transgenic Mice: A Model Neurodegeneration Caused by an Expanded CAG Trinucleotide Repeat", *Cell*, 82:937-948, 1995
	AI	Chen *et al.*, "Gene Therapy for brain tumors: Regression of experimental gliomas by adenovirus-mediated gene transfer *in vivo*", *Proc. Natl. Acad. Sci. USA*, 91:3054-3057, 1994
	AJ	Cruikshank *et al.*, "A lapidated Anti-Tat Antibody Enters Living Cells and Blocks HIV-1 Viral Replication", *Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology*, 14:193-203, 1997
	AK	Davies *et al.*, "Formation of Neuronal Intranuclear Inclusions Underlies the Neurological Dysfunction in Mice Transgenic for the HD Mutation", *Cell*, 90:537-548, 1997
	AL	DiFiglia *et al.*, "Aggregation of Huntingtin in Neuronal Intranuclear Inclusions and Dystrophic Neurites in Brain", *Science*, 277:1990-1993, 1997
	AM	Duyao *et al.*, "Inactivation of the Mouse Huntington's Disease Gene Homolog *Hdh*", *Science*, 269:407-410, 1995
	AN	Gatter *et al.*, "Transferrin receptors in human tissues: their distribution and possible clinical relevance", *J. Clin. Pathol.*, 36:539-545, 1983
	AO	Gavilondo-Cowley *et al.*, "Specific Amplification of Rearranged Immunoglobulin Variable Region Genes from Mouse Hybridoma Cells", *Hybridoma*, 9(5):407-417, 1990
	AP	Goldstein and Betz, "The Blood-Brain Barrier", *Scientific American*, pp. 74-83, 1986
	AQ	Groves and Barford, "Topological characteristics of helical repeat proteins", *Current Opinion in Structural Biology*, 9(3):383-389, 1999

Examiner Signature	Date Considered
	1/21/04

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Substitute Form PTO-1449 (Modified)	U.S. Department of Commerce Patent and Trademark Office	Attorney's Docket No. 01997-289001	Application No. 09/933,638
Information Disclosure Statement by Applicant (Use several sheets if necessary)		Applicant: Aleksey G. Kazantsev et al.	
(37 CFR §1.98(b))		Filing Date: August 20, 2001	Group Art Unit

Other Documents (include Author, Title, Date, and Place of Publication)

Examiner Initial	Desig. ID	Document
	AR	Gutekunst *et al.*, "Nuclear and Neuropil Aggregates in Huntington's Disease: Relationship to Neuropathology", *The Journal of Neuroscience*, 19(7):2522-2534, 1999
	AS	Haynes *et al.*, "Characterization of a Monoclonal Antibody (5E9) that Defines a Human Cell Surface Antigen of Cell Activation", *The Journal of Immunology*, 127(1):347-351, 1981
	AT	Hodgson *et al.*, "A YAC Mouse Model for Huntington's Disease with Full-Length Mutant Huntingtin, Cytoplasmic Toxicity, and Selective Striatal Neurodegeneration", *Neuron*, 23:181-192, 1999
	AU	Ikeda *et al.*, "Expanded polyglutamine in the Machado-Joseph disease protein induces cell death *in vitro* and *in vivo*", *Nature Genetics*, 13:196-202, 1996
	AV	Jenkins *et al.*, "Structure and Evolution of Parallel β-Helix Proteins", *Journal of Structural Biology*, 122:236-246, 1998
	AW	Kakizuka, A, "Protein precipitation: a common etiology in neuro-degenerative disorders", *Trends in Genetics*, 14(10):396-402, 1998
	AX	Kazantsev *et al.*, "Insoluble detergent-resistant aggregates form between pathological and nonpathological lengths of polyglutamine in mammalian cells", *Proc. Natl. Acad. Sci. USA*, 96:11404-11409, 1999
	AY	Klement *et al.*, "Ataxin-1 Nuclear Localization and Aggregation: Role in Polyglutamine-Induced Disease in *SCA1* Transgenic Mice", *Cell*, 95:41-53, 1998
	AZ	Larrick *et al.*, "Polymerase chain reaction using mixed primers: cloning of human monoclonal antibody variable region genes from single hybridoma cells", *Bio/Technology*, 7:934-938, 1989
	BA	Lebman *et al.*, "A Monoclonal Antibody that Detects Expression of Transferrin Receptor in Human Erythroid Precursor Cells", *Blood*, 59(3):671-678, 1982
	BB	Li *et al.*, "Ultrastructural localization and progressive formation of neuropil aggregates in Huntington's disease transgenic mice", *Human Molecular Genetics*, 8(7):1227-1236, 1999
	BC	Mangiarini *et al.*, "Exon 1 of the HD Gene with an Expanded CAG Repeat is Sufficient to Cause a Progressive Neurological Phenotype in Transgenic Mice", *Cell*, 87(1):493-506, 1996
	BD	Omary *et al.*, "Human cell-surface glycoprotein with unusual properties", *Nature*, 286(5776):888-891, 1980
	BE	Orlandi *et al.*, "Cloning immunoglobulin variable domains for expression by the polymerase chain reaction", *Proc. Natl. Acad. Sci. USA*, 86:3833-3837, 1989
	BF	Pantoliano *et al.*, "Conformational Stability, Folding, and Ligand-Binding Affinity of Single-Chain Fv Immunoglobulin Fragments Expressed in *Escherichia coli*", *Biochemistry*, 30:10117-10125, 1997
	BG	Pardridge, WM, "Receptor-Mediated Peptide Transport through the Blood-Brain Barrier", *Endocrine Reviews*, 7(3):314-330, 1986
	BH	Paulson, HL, "Human Genetics'99: Trinucleotide Repeats", *Am. J. Hum. Genet.*, 64:339-345, 1999
	BI	Perutz, MF, "Glutamine repeats and neurodegenerative diseases: molecular aspects", *Trends in Biochemical Sciences*, 24:58-63, 1999
	BJ	Reddy *et al.*, "Recent advances in understanding the pathogenesis of Huntington's disease", *Trends in Neurosci.*, 22(6):248-255, 1999
	BK	Robinson and Sauer, "Optimizing the stability of single-chain proteins by linker length and composition mutagenesis". *Proc. Natl. Acad. Sci. USA*, 95:5929-5934, 1998

Examiner Signature	Date Considered
	1/21/04

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Information Disclosure Statement by Applicant (Use several sheets if necessary) (37 CFR §1.98(b))		Applicant Aleksey G. Kazantsev et al.	
		Filing Date August 20, 2001	Group Art Unit

Other Documents (include Author, Title, Date, and Place of Publication)

Examiner Initial	Desig. ID	Document
	BL	Ross, CA, "Intranuclear Neuronal Inclusions: A Common Pathogenic Mechanism for Glutamin-Repeat Neurodegenerative Diseases", *Neuron*, 19:1147-1150, 1997
	BM	Saudou *et al.*, "Huntingtin Acts in the Nucleus to Induce Apoptosis but Death Does Not Correlate with the Formation of Intranuclear Inclusions", *Cell*, 95:55-66, 1998
	BN	Scherzinger *et al.*, "Self-assembly of polyglutamine-containing huntingtin fragments into amyloid-like fibrils: Implications for Huntington's disease pathology", *Proc. Natl. Acad. Sci. USA*, 96:4604-4609, 1999
	BO	Sutherland *et al.*, "Ubiquitous cell-surface glycoprotein on tumor cells is proliferation-associated receptor for transferring", *Proc. Natl. Acad. Sci. USA*, 78(7):4515-4519, 1981
	BP	Zeitlin *et al*, "Increased apoptosis and early embryonic lethality in mice nullizygous for the Huntington's disease gene homologue", *Nature Genetics*, 11:155-163, 1995
	BQ	Zhuchenko *et al.*, "Autosomal dominant cerebellar ataxia (SCA6) associated with small polyglutamine expansions in the α_{1A}-voltage-dependent calcium channel", *Nature Genetics*, 15:62-69, 1997
	BR	

Examiner Signature	Date Considered 1/21/04

EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US01/26097

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) :C12Q 1/68; C12N 15/82
US CL : 435/7.1; 530/350

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/7.1; 530/350

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

A_GENESEQ; ISSUED PATENTS;PIR_68; SPTREMBL

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

STN: BIOSIS, MEDLINE, WPIDS, HCAPLUS, JAPIO

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 93/15213 A1 (ZENECA LIMITED) 05 August 1993 (05.08.93). See entire document.	1-11
Y	Database GenCore on STN, AN AAR95976, WEININGER et al. WO 96/17956 (THE GENE POOL, INC.) 13 June 1996 (13.06.96). See entire document.	1-11

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search 17 DECEMBER 2001	Date of mailing of the international search report 24 JAN 2002
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer HOPE ROBINSON Telephone No. (703) 308-0196

Form PCT/ISA/210 (second sheet) (July 1998)★

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US01/26097

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

Please See Extra Sheet.

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-11

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US01/20097

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING
This ISA found multiple inventions as follows:

Group I, claim(s)1-11, drawn to a therapeutic agent.
Group II, claim(s) 12-14, drawn to an isolated DNA molecule.
Group III, claim(s) 15-17, drawn to a method of treating a patient who has a disease associated with expanded CAG.

The inventions listed as Groups I-III do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The invention of Group I do not escape the prior art as the therapeutic agent which comprises the domain set forth in SEQ ID NO: 11 is taught by Weininger et al. (WO 96/617956, 13 June 1996, see the sequence alignment). Therefore, the claimed invention lacks a special technical feature. Furthermore, the method of Group III do not make or use the therapeutic agent of Group I.